

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 November 2000 (03.11.00)	
International application No. PCT/US00/06244	Applicant's or agent's file reference 4239-54280
International filing date (day/month/year) 10 March 2000 (10.03.00)	Priority date (day/month/year) 10 March 1999 (10.03.99)
Applicant GE, Hui	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

29 September 2000 (29.09.00)

in a notice effecting later election filed with the International Bureau on:

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  S. Mafla  Telephone No.: (41-22) 338.83.38
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**(19) World Intellectual Property Organization  
International Bureau**



**(43) International Publication Date  
14 September 2000 (14.09.2000)**

**PCT**

**(10) International Publication Number  
WO 00/54046 A3**

- (51) International Patent Classification<sup>7</sup>:** G01N 33/543, 33/68
- (21) International Application Number:** PCT/US00/06244
- (22) International Filing Date:** 10 March 2000 (10.03.2000)
- (25) Filing Language:** English
- (26) Publication Language:** English
- (30) Priority Data:**  
60/123,586 10 March 1999 (10.03.1999) US
- (71) Applicant (for all designated States except US):** THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES, THE NATIONAL INSTITUTES OF HEALTH [US/US]; Office of Technology Transfer, Suite #325, 6011 Executive Boulevard, Rockville, MD 20852 (US).
- (72) Inventor; and**
- (75) Inventor/Applicant (for US only):** GE, Hui [CN/US]; 437 Upshire Circle, Gaithersburg, MD 20878 (US).
- (74) Agent:** NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Whinston, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).

**(81) Designated States (national):** AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

**(84) Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— With international search report.

**(88) Date of publication of the international search report:**  
21 December 2000

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**WO 00/54046 A3**

**(54) Title:** UNIVERSAL PROTEIN ARRAY SYSTEM

**(57) Abstract:** This invention relates to ordered arrays of molecules, for instance polypeptides or proteins. Such arrays, referred to as universal protein arrays, are described in both macro- and microarray formats. Methods of production and use of such arrays are also described. Also disclosed are kits for the use of such arrays and the preparation of probes for use with them.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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EE	Estonia						

## INTERNATIONAL SEARCH REPORT

Inte [REDACTED] Application No  
PCT/US00/06244

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 G01N33/543 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data, BIOSIS, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	<p>MEDLINE, Washington DC USA; abstract no. 20075324, abstract XP002144063. &amp; H. GE : "UPA, a universal protein array system for quantitative detection of protein-protein, protein-DNA, protein-RNA and protein-ligand interactions." NUCLEIC ACID RESEARCH, vol. 28, no. 2, 15 January 2000 (2000-01-15), page e3 Bethesda MD USA</p> <p>—</p> <p style="text-align: center;">-/-</p>	1-42

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

4 August 2000

01/09/2000

Name and mailing address of the ISA

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Van Bohemen, C

## INTERNATIONAL SEARCH REPORT

Int'l filing date Application No.  
PCT/US 00/06244

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 063 810 A (CIBA-GEIGY AG) 3 November 1982 (1982-11-03)  figure 1; examples 1-14	1-21, 24-30, 33-42
Y		1-42
X	EP 0 818 467 A (NEC CORPORATION) 14 January 1998 (1998-01-14)  claims 1-38	1-21, 24-30, 33-42
Y		1-42
X	MEDLINE, Washington DC USA; abstract no. 97348061, abstract XP002144064 & E. ADACHI ET AL.: "Assembly process of 2D protein arrays in wetting films." ADVANCES IN BIOPHYSICS, vol. 34, 1997, pages 81-92, Japan	13, 24

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

Int'l	loc.	Application No
PCT/US 90/06244		

Patent document cited in search report	Publication date	Patent family member(s)		Publication date	
EP 63810	A	03-11-1982	AR AT AU AU BR CA CY DE DK ES ES ES ES ES FI GB GR HK IE IL JP JP MX NO NZ PH PT SG US ZA	231590 A 18463 T 560790 B 8306982 A 8202492 A 1200761 A 1437 A 3269567 D 189182 A, B, 511735 D 8400199 A 523722 D 8405156 A 523723 D 8405157 A 821441 A, B, 2099578 A, B 75430 A 53888 A 53295 B 65627 A 58009070 A 160043 A 821411 A, B, 200443 A 26773 A 74816 A, B 25288 G 5486452 A 8202896 A	28-12-1984 15-03-1986 16-04-1987 04-11-1982 12-04-1983 18-02-1986 10-03-1989 10-04-1986 30-10-1982 16-10-1983 01-01-1984 16-05-1984 01-09-1984 16-05-1984 01-09-1984 30-10-1982 08-12-1982 17-07-1984 22-07-1988 12-10-1988 29-11-1985 19-01-1983 09-11-1989 01-11-1982 12-07-1985 28-09-1992 01-05-1982 15-07-1988 23-01-1996 29-12-1982
EP 818467	A	14-01-1998	JP	10025299 A	
				27-01-1998	

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

REC'D 27 JUN 2001
WIPO PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference  4239-54280	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/US00/06244	International filing date (day/month/year)  10/03/2000	Priority date (day/month/year)  10/03/1999
International Patent Classification (IPC) or national classification and IPC  G01N33/48		
<p>Applicant  THE GOVERNMENT OF THE UNITED STATES OF AMERICA...</p> <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p style="text-align: center;">3</p> <p>These annexes consist of a total of sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V    <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input checked="" type="checkbox"/> Certain documents cited</li> <li>VII   <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>		

Date of submission of the demand  29/09/2000	Date of completion of this report  25.06.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer  Van Bohemen, C  Telephone No. +31 70 340 2199



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/06244

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-32                   as originally filed

**Claims, No.:**

1-45                   as received on                   17/02/2001 with letter of                   16/02/2001

**Drawings, sheets:**

1/4-4/4               as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,               pages:
- the claims,                   Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/06244

the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 1-45  
No: Claims

Inventive step (IS) Yes: Claims  
No: Claims 1-45

Industrial applicability (IA) Yes: Claims 1-45  
No: Claims

2. Citations and explanations  
**see separate sheet**

**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**VII. Certain defects in the international application**

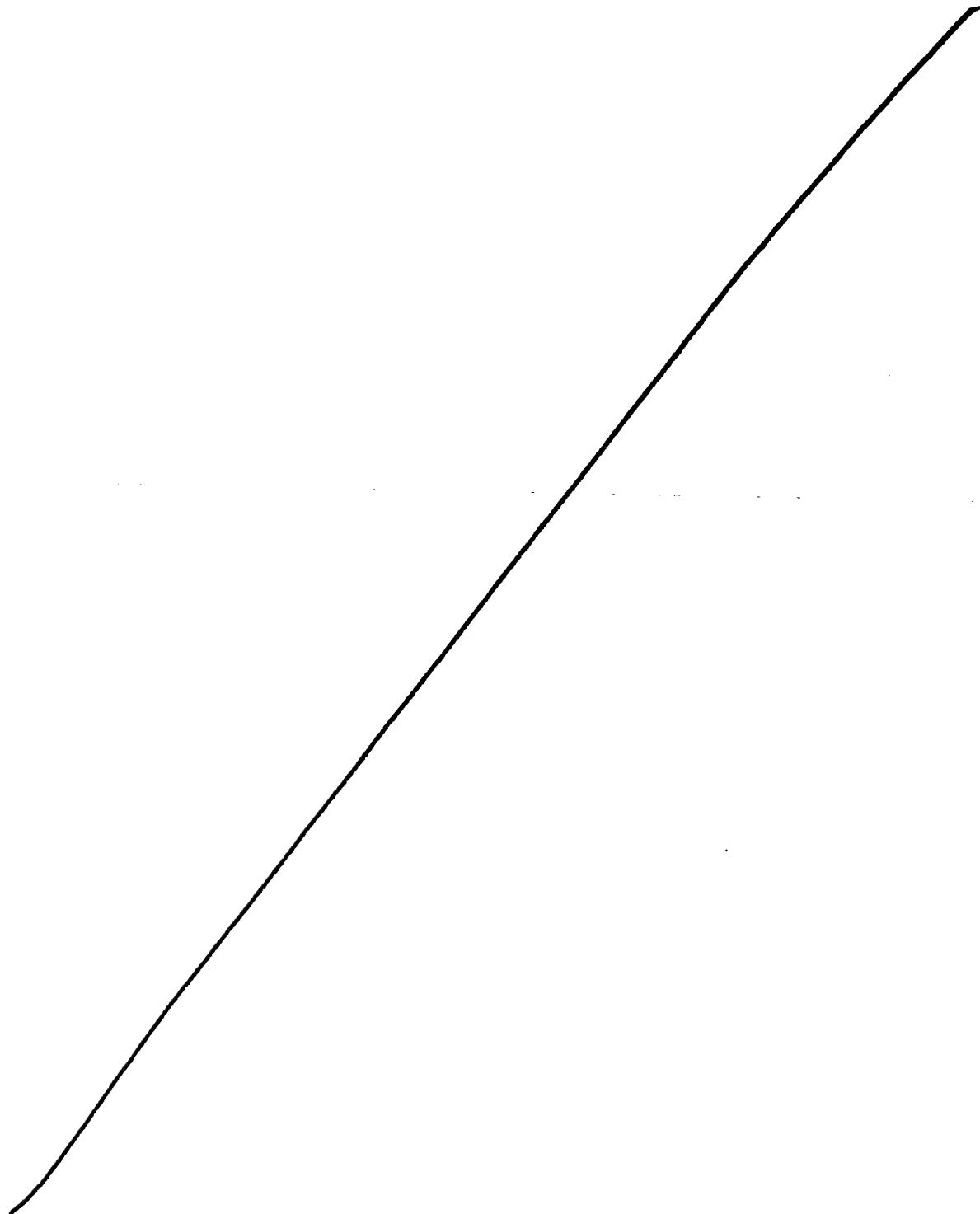
The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/06244



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/06244

**R It m V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following document, which has been cited as an "X - document" in the international search report:

D1: EP-A- 818467 (NEC CORPORATION )

The present application (PA) does not meet the requirements of Article 33(1) and (3) and Rule 64 PCT, because the subject-matter of claims 1-45 does not appear to be inventive.

Document D1 is identified as the closest prior art (CPA). By his own admission (cf. Statement under Article 34 PCT) the applicant confirms that D1 discloses aligned peptide arrays with a plurality of peptide segments and methods using said arrays. Claims 1-45 of the PA differ from this by using full length polypeptide molecules rather than polypeptide segments.

In consequence, the objective problem identified by the PA is identified as follows: the provision of further peptide arrays and methods using said arrays.

The solution is identified as follows: use full length polypeptide molecules.

Departing from the CPA document D1, it would appear that the artisan would find himself in a one-way street situation: the artisan would be unavoidably propelled to use full length polypeptide molecules on arrays in addition to polypeptide segments. There would be a reasonable expectation of success. Hence, the use full length polypeptide molecules on arrays would appear to be obvious to the artisan without involving an inventive step (cf. Art. 33(1) and (3) and Rule 64 PCT).

Incorporation of the subject-matter of dependent claims 2-13 and 45, or 15-25 or 27-34 or 36 and 37 or 39-44 into anyone of the independent claims 1, 14, 26, 35 or 40 would not render these claims inventive, because the subject-matter of these dependent claims appears to be one of the straight forward possibilities from which the

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/06244

artisan would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.

In summary, as presently formulated novelty and industrial applicability could apparently be recognized, but the inventivity of claims 1-45 can apparently not be recognized (cf. 33(1) and (3) and Rule 64 PCT).

**Re Item VI**

**Certain documents cited**

Depending on whether or not the present application validly claims a priority date earlier than the international filing date, the following document, which was cited in the international search report, might be considered in the course of further procedures.

H. Ge (15-1-2000). UPA, a universal protein array system for quantitative detection of protein-protein, protein-DNA, protein-RNA and protein-ligand interactions. Nucleic Acids Res, 28 (2), e3i - e3vii.

**Re Item VII**

**Certain defects in the international application**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 has not been mentioned in the description, nor has this document been identified therein.

**Re Item VIII**

**Certain observations on the international application**

1. Although claims 14, 23, 35, 38 and 40 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter. It would appear that conciseness and clarity ex art. 6 PCT could be enhanced by defining the relevant subject-matter in terms of a single independent claim, followed by dependent claims

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/06244

covering features which are merely optional.

2. Claims 1, 2, 4, 21, 30 and 33 are not clear ex art. 6 PCT, because the term "substantially pure" is not clear; the artisan would not automatically understand which degree of purity is intended.
3. Claim 1 is not clear ex art. 6 PCT, because the term "addressable pattern" is not clear; the artisan would not automatically understand which pattern is intended.
4. Claim 6 is not clear ex art. 6 PCT, because the term "computer readable format" is not clear; the artisan would not automatically understand which format is intended.
5. Claim 10, 19, 28, 36 and 42 are not clear ex art. 6 PCT, because the term "microarray" is not clear; the artisan would not automatically understand which size is intended.
6. Claim 26 is not clear ex art. 6 PCT, because the term "instructions" is not clear in the context of said claim; the artisan would not automatically understand which technical features are intended. For completeness it is noted that "instructions" are not regarded as a characterizing technical feature of the kit of claim 26 of the PA. The applicant is required to indicate which features always and unambiguously distinguish his kit from those disclosed in the prior art.
7. The vague and imprecise statement in the description on page 32, last line, implies that the subject-matter for which protection is sought may perhaps be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>4239-54280</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/06244</b>	International filing date ( <i>day/month/year</i> ) <b>10/03/2000</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>10/03/1999</b>
Applicant <b>THE GOVERNMENT OF THE UNITED STATES OF AMERICA...</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable** (See Box I).

3.  **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**UNIVERSAL PROTEIN ARRAY SYSTEM**

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.